

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A process for differentiating primate pluripotent stem (pPS) cells into mature hepatocytes ~~hepatocyte-lineage-cells~~ in at least three discrete steps, comprising:

- a) culturing undifferentiated pPS cells with a means for causing differentiation of the cells into cells having characteristics of fetal endoderm;

- b) culturing the cells from a) with a means for causing differentiation of fetal endoderm cells into cells having characteristics of hepatocyte progenitor cells;

- c) culturing the cells from b) with a means for causing differentiation of hepatocyte progenitor cells into cells having characteristics of mature hepatocytes;

thereby producing a cell population that has at least five of the following characteristics:

- antibody-detectable expression of α_1 -antitrypsin (AAT);
- antibody-detectable expression of albumin;
- absence of antibody-detectable expression of α -fetoprotein;
- RT-PCR detectable expression of asialoglycoprotein receptor (ASGR);
- evidence of glycogen storage;
- evidence of cytochrome p450 enzyme activity;
- evidence of glucose-6-phosphatase enzyme activity; and

- the morphological features of hepatocytes.

2. (Currently amended) The process of claim 1, wherein the culturing in a) produces a cell population comprising ~~in which most of the cells~~ expressing express at least three markers selected from Hex, Sox17, HNF 3a, HNF 3b, and α fetoprotein (AFP).
3. (Currently amended) The process of claim 1, wherein the culturing in b) produces a cell population comprising ~~in which most of the cells~~ expressing express at least three markers selected from γ -glutamyl tranpeptidase, HNF 4a isomer a7/a8, albumin, α 1 antitrypsin (AAT), and Matripase 2.
4. (Currently amended) The process of claim 1, wherein the culturing in c) produces a cell population comprising ~~in which most of the cells~~ expressing express at least three markers selected from ApoCII, tyrosine oxygenase (TO), CYP3A4, CYP3A7, HNF 4a isomer a1/a2, and LST 1.
5. (Currently amended) The process of claim 1, wherein a) comprises culturing the cells with media comprising one of the following: DMSO, fibroblast growth factor 8 (FGF 8), or a bone morphogenic protein (BMP).
6. (Currently amended) The process of claim 1, wherein b) comprises culturing the cells with media comprising one of the following: a histone deacetylase

inhibitor, a BMP, epidermal growth factor (EGF), a corticosteroid, or Oncostatin M.

7. (Currently amended) The process of claim 1, wherein c) comprises culturing the cells with media comprising one of the following: hepatocyte growth factor (HGF), or with one or more growth factors in combination with a histone deacetylase inhibitor.
8. (Currently amended) The process of claim 1, comprising culturing the undifferentiated cells with DMSO, then with butyrate in the absence of growth factors, then with butyrate in combination with one or more growth factors.
9. (Currently amended) The process of claim 1, comprising culturing the undifferentiated cells with DMSO, then with one or more growth factors in combination with Oncostatin M, optionally in the presence of a corticosteroid, then with HGF.
10. (Currently amended) The process of claim 1, comprising culturing the undifferentiated cells with a BMP, then with Oncostatin M, optionally in the presence of a BMP or a corticosteroid, then with HGF.
11. (Currently amended) A process for differentiating human embryonic stem (hES) cells into hepatocyte lineage cells, comprising:

- a) culturing the undifferentiated pluripotent cells with DMSO,
 - b) culturing the cells from a) with a histone deacetylase inhibitor in the absence of growth factors; and then
 - c) culturing the cells from b) with a histone deacetylase inhibitor in combination with one or more growth factors thereby differentiating human embryonic stem (hES) cells into hepatocyte lineage cells.
12. (Original) The process of claim 11, wherein the histone deacetylase inhibitor is n butyrate.
13. (Currently amended) A process for differentiating human embryonic stem (hES) cells into hepatocyte lineage cells, comprising:
- a) culturing undifferentiated hES cells with DMSO;
 - b) culturing the cells from a) with one or more growth factors in combination with Oncostatin M; and then
 - c) culturing the cells from b) with hepatocyte growth factor (HGF) thereby differentiating human embryonic stem (hES) cells into hepatocyte lineage cells.
14. (Original) The process of claim 13, wherein a) comprises culturing the cells with FGF 1, FGF 2, FGF 4 or FGF 8.
15. (Original) The process of claim 13, wherein b) comprises culturing the cells with EGF or FGF in combination with Oncostatin M and dexamethasone.

16. (Currently amended) A process for differentiating human embryonic stem (hES) cells into hepatocyte lineage cells, comprising:
- a) culturing undifferentiated hES cells with FGF 8 or a bone morphogenic protein (BMP);
 - b) culturing the cells from a) with Oncostatin M, and then
 - c) culturing the cells from b) with HGF thereby differentiating human embryonic stem (hES) cells into hepatocyte lineage cells.
17. (Original) The process of claim 16, wherein a) comprises culturing the cells with at least two bone morphogenic proteins selected from BMP 2, BMP 4, and BMP 7, optionally in the presence of dexamethasone.
18. (Original) The process of claim 16, wherein b) comprises culturing the cells with a BMP, dexamethasone, or nerve growth factor (NGF).
19. (Withdrawn) A system for generating hepatocyte lineage cells, comprising a cell population produced by the process of claim 1, wherein the system further comprises the pPS cell line used to produce said cell population according to the process.
20. (Withdrawn) A system for generating hepatocyte lineage cells, comprising a cell population produced by the process of claim 16, wherein the system further

comprises the pPS cell line used to produce said cell population according to the process.

21. (Original) The process of claim 1, wherein the pPS cells are obtained from a human blastocyst, or are the progeny of such cells.

22. (Original) The process of claim 1, wherein the pPS cells are human embryonic stem cells.